

### **REMARKS**

Claims 1-29 constitute the pending claims in the present application, and claims 1, 2, 5, 6, 9, 10, 13-25, 28, and 29 are currently under consideration. Applicants cancel, without prejudice, claims 28 and 29. Applicants reserve the right to prosecute claims of similar or differing scope. Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

1. The specification was objected to for allegedly failing to satisfy the requirements for receiving the benefit of an earlier priority date. Applicants' amendments to the specification are believed to obviate the objection. Applicants' amendments are supported by the "Request for Filing of a Continuation Application of an International Application" filed March 12, 2001 (see, page 1, box 7 of form PTO/SB/13/PCT). Reconsideration and withdrawal of this objection are requested.

2. The drawings were objected to for allegedly failing to comply with 37 CFR 1.84(p)(5). Applicants' amendment to the specification is believed to obviate the objection. Reconsideration and withdrawal of the objection are respectfully requested.

3. Claims 1, 2, 6, 9, 10, 18, 20-23, 28, and 29 are rejected under 35 U.S.C. 112, second paragraph, as indefinite for allegedly failing to particularly point out the claimed subject matter. Applicants traverse this rejection and contend that the rejection is moot in light of the amended claims. Applicants' amendments are not in acquiescence to the rejection, and Applicants reserve the right to prosecute claims of similar or differing scope.

(a) Claim 1 was rejected for allegedly omitting essential steps. Applicants' amendments to claim 1 are believed to obviate the rejection. Reconsideration and withdrawal are requested.

(b) Claims 2 and 6 were rejected for failing to particularly point out the anti-hedgehog antibody homologs. Applicants have amended the claims to more particularly point out the anti-hedgehog antibody homologs for use in the claimed methods. In light of Applicants' amendments, one of skill in the art could readily appreciate the metes and bounds of the claimed subject matter. Reconsideration and withdrawal are requested.

(c) Claim 9 was rejected for allegedly lacking clarity. Applicants have amended claim 9 to more particularly point out that proliferation of hair follicle keratinocytes is inhibited by the agent. Applicants' amendment is made solely for clarity and does not narrow the scope of the claim. Reconsideration and withdrawal are requested.

(d) Claim 18 was rejected for allegedly lacking clarity. Applicants have amended claim 18 to clarify that the therapeutic comprises the agent, and that this therapeutic agent inhibits growth of the cells. Additionally, Applicants similarly amended claim 19 which was phrased similarly to previously pending claim 18. Applicants' amendments are made solely for clarity and do not narrow the scope of the claims. Reconsideration and withdrawal of the rejection are requested.

(e) Claim 28 was rejected for allegedly failing to particularly point out the claimed subject matter. Applicants' cancellation of claim 28 renders the rejection moot.

4. Claims 1, 5, 9, 13-20, and 24 are rejected under 35 U.S.C. 102(e) as allegedly anticipated by US Patent No. 6,639,051 (the "'051 patent"). Applicants traverse this rejection and contend that the rejection is moot in light of the amended claims.

To expedite prosecution, Applicants have amended the claims to specifically point out that the hedgehog antagonist for use in the present methods is an anti-hedgehog antibody. In other words, Applicants have amended the claims to incorporate the novel features of previously pending claims 2, 6, 10, and 25, thereby obviating the rejection. As the Examiner has already acknowledged, the '051 patent does not teach the use of anti-hedgehog antibodies, and thus the '051 patent fails to teach each and every limitation of the pending claims.

Applicants' amendments are not in acquiescence to the rejection. Applicants reserve the right to prosecute claims of similar or differing scope. Reconsideration and withdrawal of this rejection are respectfully requested.

5. Claims 28 and 29 are rejected under 35 U.S.C. 102(b) as allegedly anticipated by Ericson et al. Applicants traverse this rejection and contend that the rejection is moot in light of the amended claims.

To expedite prosecution, Applicants have canceled claims 28 and 29, thereby rendering the rejection moot. Cancellation of claims 28 and 29 are not in acquiescence to the rejection, and Applicants reserve the right to prosecute claims of similar or different scope. Reconsideration and withdrawal of this rejection are requested.

6. Claims 2, 6, 10, 21-23, and 25 are rejected under 35 U.S.C. 103(a) as allegedly unpatentable over the '051 patent in view of Ericson et al. and US Patent No. 4,816,567 (the "'567 patent"). Applicants traverse this rejection and contend that the rejection is moot in light of the amended claims.

To establish a *prima facie* case of obviousness, one of skill in the art must have been motivated to combine the cited references to arrive at an invention that meets each and every limitation of the pending claims. These requirements have not been satisfied here. Specifically, as indicated in MPEP 2143.01, "[t]he mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination."

As indicated by the Examiner, Wang et al. teach methods for administering hedgehog agonists, as well as methods for administering hedgehog antagonists. Wang et al. "does not however specifically teach that the hedgehog antagonist be an anti-hedgehog antibody." (Office Action, page 6).

The Examiner cites Ericson et al. as teaching that anti-hedgehog antibodies can be used as antagonists of hedgehog signaling. However, Ericson et al. merely provide that anti-hedgehog antibodies antagonize hedgehog signaling in a particular in vitro neuronal tissue explant system (e.g., floor plate explants). The teachings of Ericson et al. provide no motivation to extend the results gathered in a particular in vitro neuronal explant system to non-neuronal systems such as hair. Absent motivation to combine the references, the combination of Wang et al. and Ericson et al. fail to satisfy the criteria necessary for rendering the claimed invention obvious.

Additionally, Applicants point out that the presently claimed methods encompass several distinct physiological effects caused by administration of anti-hedgehog antibodies: inhibition of growth or differentiation of epithelial cells; inhibition of proliferation of epithelial cells;

inhibition of hair growth; and inhibition of proliferation of hair follicle cells. Neither Wang et al. nor the combination of Wang et al. and Ericson et al. teach or suggest that anti-hedgehog antibodies could have these effects on non-neuronal cells and tissues; as required by the pending claims.

The Examiner additionally cited US Patent No. 4,816,567 (the “‘567 patent”) which, in combination with Wang et al. and Ericson et al., allegedly renders the claimed invention obvious. As outlined in detail above, to render an invention obvious, there must be some motivation to combine the cited references. Such motivation does not exist here. The ‘567 patent provides general teachings directed to making chimeric antibodies. The ‘567 patent does not teach or suggest anti-hedgehog antibodies, or that anti-hedgehog antibodies can be used to antagonize hedgehog signaling. Furthermore, the ‘567 patent does not teach or suggest that hedgehog antagonists generally, or anti-hedgehog antibodies specifically, can be used to modulate any of the following physiological activities: inhibition of the growth or differentiation of epithelial cells; inhibition of the proliferation of epithelial cells; inhibition of hair growth; and inhibition of the proliferation of hair follicle cells. Given that the general teachings of the ‘567 patent are entirely unrelated to the subject matter of the present application, one of skill in the art would have no motivation to combine this reference with either Wang et al. or Ericson et al.

Applicants contend that the combination of references cited by the Examiner is insufficient to render the claimed invention obvious. Reconsideration and withdrawal of this rejection is respectfully requested.

As outlined in detail above, Applicants contend that the cited combination of references fail to render the claimed invention obvious because one of skill in the art would have had no motivation to combine the cited references. Additionally, Applicants point out that a valid patent may issue for a nonobvious species related to a prior patented invention. Applicants assert that the presently claimed invention is a species which is nonobvious and patentable over the cited references.

Applicants contend that the cited references fail to teach or suggest the particular combination of elements set forth in the claims. Specifically, the cited references fail to teach or suggest methods for using anti-hedgehog antibodies (the particular composition recited in the

pending claims) to inhibit cells of particular tissues, for example hair follicle cells. These references fail to teach the benefits of the particular combination of agents and target cell types set forth in the pending claims. Furthermore, these references provide no motivation to specifically select the particular elements (i.e., the particular hedgehog antagonists and target cell types), as presently claimed. MPEP 2144.08 outlines the guidelines for determining that a reference renders an invention obvious and directs the Examiner to “determine whether one of ordinary skill in the relevant art would have been motivated to make the claimed invention as a whole, i.e., to select the claimed species or subgenus from the disclosed prior art genus.” Applicants contend that the cited references fail to provide motivation to select the specific hedgehog antagonists and the specific target cell types, as required by the pending claims.

For the foregoing reasons, Applicants contend that the cited references fail to satisfy the criteria necessary for rendering the claimed invention obvious. To expedite prosecution of claims directed to commercially relevant subject matter, Applicants have amended the claims to more particularly point out the particular hedgehog antagonists for use in the presently claimed methods. Applicants’ amendments are not in acquiescence to the rejection, and Applicants reserve the right to prosecute claims of similar or differing scope. In light of Applicants’ arguments and amendments, reconsideration and withdrawal of this rejection is requested.

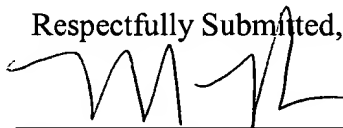
### CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945, under order no. CIBT-P01-114.**

Date: December 7, 2004

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Respectfully Submitted,



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